Published in final edited form as:

Mach Learn Med Imaging. 2011 ; 7009: 1–9. doi:10.1007/978-3-642-24319-6_1.

Learning Statistical Correlation of Prostate Deformations for Fast Registration

Yonghong Shi^{1,2}, Shu Liao¹, and Dinggang Shen¹

Dinggang Shen: dgshen@med.unc.edu

¹IDEA Lab, Department of Radiology and BRIC, University of North Carolina at Chapel Hill

²Digital Medical Research Center, Shanghai Key Lab of MICCAI, Fudan University, China

Abstract

This paper presents a novel fast registration method for aligning the planning image onto each treatment image of a patient for adaptive radiation therapy of the prostate cancer. Specifically, an online correspondence interpolation method is presented to learn the statistical correlation of the deformations between prostate boundary and non-boundary regions from a population of training patients, as well as from the online-collected treatment images of the same patient. With this learned statistical correlation, the estimated boundary deformations can be used to rapidly predict regional deformations between prostates in the planning and treatment images. In particular, the population-based correlation can be initially used to interpolate the dense correspondences when the number of available treatment images from the current patient is small. With the acquisition of more treatment images from the current patient, the patient-specific information gradually plays a more important role to reflect the prostate shape changes of the current patient during the treatment. Eventually, only the patient-specific correlation is used to guide the regional correspondence prediction, once a sufficient number of treatment images have been acquired and segmented from the current patient. Experimental results show that the proposed method can achieve much faster registration speed yet with comparable registration accuracy compared with the thin plate spline (TPS) based interpolation approach.

Keywords

Adaptive radiation therapy; Fast registration; Patient-specific statistical correlation; Canonical correlation analysis

1 Introduction

Prostate cancer is the second-leading cause of cancer death for American men [1]. External beam radiation therapy is often used for prostate cancer treatment [2] by spreading the treatment over a weeks-long series of daily fractions. Since the prostate is surrounded by healthy tissue that can also be harmed by radiation, it is important to maximize the harm to the cancer while minimize the harm to healthy tissue. In addition, for adaptive radiation

therapy, it is important to adjust the treatment plan by updating beam intensities and shapes according to the estimated patient position and motion from the acquired images [3, 4]. All of these tasks need image segmentation and registration for prostate, as studied extensively in the literature.

In particular, image registration is able to estimate prostate deformation during radiotherapy. Thus with registration between the planning image and each treatment image, the treatment plan determined in the planning image space can be warped onto the treatment image space, and also the dose distribution map in the treatment image space can be warped back onto the planning image space for measurement of the actual total dose delivered to the patient after a portion of the treatment [5–7].

To achieve this goal, the segmented prostate in the planning image should be fast registered onto the prostate in each treatment day or vice versa. However, there are two difficulties with current registration algorithms. First, due to the limited contrast of CT images around the prostate boundaries, it is very difficult for the intensity-based registration algorithms to differentiate the corresponding structures in the planning and treatment images [5, 6]. Second, it is also difficult to perform fast registration by using the conventional intensity-based registration algorithms [7, 8], or even using the interpolation algorithms such as thin plate spline (TPS) [9] when the number of correspondences in the prostate boundaries or the size of region of interest (ROI) become large.

Therefore, in this paper, we present a novel fast registration method, which can learn the statistical correlation of the deformations between prostate boundary and non-boundary regions from the training patients, as well as from the online-collected treatment images of the current patient. With the learned statistical correlation, the estimated boundary correspondences can be used to rapidly predict the non-boundary regional correspondences between prostates in the planning and treatment images. Also, the patient-specific correlation information can be updated online to reflect the prostate shape changes during the treatment. The proposed method is detailed below.

2 Method

2.1 Description

Statistical shape-based segmentation algorithm [10] can *not only* segment the prostate from the planning and treatment images, *but also* obtain boundary correspondences between all segmented prostate shapes. To establish dense correspondences (or transforms) for the points around the prostate shapes, the use of correspondence interpolation algorithms such as TPS is needed. However, these algorithms are generally slow and not efficient for clinical application.

Actually, the statistical correlation between the boundary correspondences and non-boundary regional correspondences can be learned from a population of training patients, as well as available treatment images of the current patient. Then, this learned correlation can be used to guide the estimation of dense correspondences for the non-boundary regions around the prostate. In the following, we will detail this idea. In particular, Section 2.2 will

first introduce how to learn the statistical correlation from a population of training patients. Then, Section 2.3 will introduce how to learn the patient-specific correlation from a patient, and also how to use the patient-specific correlation to gradually replace the population information for more effective interpolation of dense correspondences for prostate.

2.2 Learning Statistical Correlation from a Population of Training Patients

Training Samples—Given a number of prostate samples segmented from serial images of training patients, the boundary correspondences across different prostate shapes can be established by the deformable shape model [10]. Similarly, we can estimate the correspondences for the prostate shape segmented from the planning image of the current patient. In this way, we can use the established correspondences to warp the prostate shapes of each training patient onto the planning image space of the current patient, for obtaining the aligned prostate shapes.

Let us assume that we have P training patients $\{S^i | i = 1, \dots, P\}$. Each patient has d_i segmented prostate images $\{S_j^i | i = 1, \dots, P; j = 1, \dots, d_i\}$, where each image is represented by a shape with M points, i.e., $S_j^i = \{(x_{j,l}^i, y_{j,l}^i, z_{j,l}^i) | l = 1, \dots, M\}$. We can linearly align each prostate shape S_j^i of the i -th training patient onto the prostate shape S_1^0 of the planning image of the current patient S^0 , for obtaining its aligned prostate shape $S_{j \rightarrow 1}^i$ in the planning image space of the current patient. Based on all aligned prostate shapes $\{S_{j \rightarrow 1}^i\}$ from each patient S^i , we can calculate their mean shape $\bar{S}^i = \sum_{j=1}^{d_i} S_{j \rightarrow 1}^i / d_i$, and then obtain the residual deformation $B_j^i = S_{j \rightarrow 1}^i - \bar{S}^i$ from each aligned prostate shape $S_{j \rightarrow 1}^i$ by subtracting the mean prostate $\bar{S}^i$ from $S_{j \rightarrow 1}^i$. Thus, based on the prostate shape in the planning image S_1^0 of the current patient S^0 and the learned residuals from different samples of training patients, we can obtain various deformed prostate shapes, $\{C_j^i = B_j^i + S_1^0 | i = 1, \dots, P; j = 1, \dots, d_i\}$, to simulate possible prostate deformations for the current patient during the treatment.

Then, by using a correspondence interpolation algorithm, i.e., TPS [11], we can interpolate N dense regional correspondences for each deformed prostate shape C_j^i . Accordingly, we can get many paired samples for boundary correspondences and non-boundary regional correspondences, i.e., $\{(C_j^i, R_j^i) | i = 1, \dots, P; j = 1, \dots, d_i\}$, where C_j^i is the $3M$ -dimensional vector and R_j^i is the $3N$ -dimensional vector. With this training set, we can first perform principal component analysis (PCA) to get a compact representation for the boundary correspondences by using all samples $\{C_j^i | i = 1, \dots, P; j = 1, \dots, d_i\}$, as well as for the non-boundary correspondences using the samples $\{R_j^i | i = 1, \dots, P; j = 1, \dots, d_i\}$ as described in Equations (1) and (2) below.

$$C_j^i = \bar{C} + \varphi_C \alpha_j^i \quad (1)$$

$$R_j^i = \bar{R} + \varphi_R \beta_j^i \quad (2)$$

Where $\bar{C}$ and $\bar{R}$ denote the respective means for $\{C_j^i\}$ and $\{R_j^i\}$, with ϕ_C and ϕ_R as the respective eigenvector matrices. α_j^i and β_j^i denote the respective reconstruction coefficient vectors for $\{C_j^i\}$ and $\{R_j^i\}$. Thus, each prostate shape C_j^i can be represented by a small number of coefficients, i.e., a coefficient vector α_j^i , and each non-boundary regional correspondence sample can also be represented by a coefficient vector β_j^i . We can then estimate the correlation between the coefficient vectors α_j^i and β_j^i by using canonical correlation analysis (CCA) [11].

CCA-based Prediction—CCA explores the correlative structures of two sets of variables, i.e., α_j^i and β_j^i in our application. The canonical correlation is the correlation of two canonical (latent) variables, one variable representing a set of independent variables, and the other representing a set of dependent variables. The canonical correlation is optimized such that the linear correlation between the two latent variables is maximized. Mathematically, CCA extracts the correlated modes between vectors α_j^i and β_j^i by seeking a set of transformation vector pairs, A_k and B_k , which yields the canonical variates u_k and v_k with maximum correlation as follows:

$$u_k = (\alpha_j^i)^T A_k \quad (3)$$

$$v_k = (\beta_j^i)^T B_k \quad (4)$$

With estimation of canonical variates u_k and v_k , we can estimate their correlation and use it for prediction. For instance, given a new prostate shape segmented from a new treatment image of the current patient at t -th time-point $S_{t \rightarrow 1}^0$, we can first obtain its PCA-based coefficient vector α_t^0 according to Equation (1), and then obtain the corresponding canonical variates v_k using Equation (3). The estimation of the canonical variates v_k is in the canonical space. The linear regression is used for the estimation of v_k from u_k [11]. Then, we can estimate the coefficient vector β_t^0 for the non-boundary regional correspondences using Equation (4), and use the reversed PCA to eventually estimate the regional correspondences for the prostate in the new treatment image R_t^0 by Equation (2).

2.3 Refining Interpolation of Dense Correspondences by Patient-Specific Information

For each treatment image of the current patient, we can first segment the prostate shape, and then establish the correspondences between the prostate in the planning image and the prostate in the treatment image. The new pairs of correspondences in the prostate boundaries and the non-boundary region around the prostate can be used to train a patient-specific correlation model between the deformations of the prostate boundaries and non-boundary

regions. Since this model is more patient specific, its contribution should become larger than that from the population of training patients, once enough treatment images have been collected from the current patient.

Assume that we have $t - 1$ segmented prostate images $\{S_j^0 | j=1, \dots, t-1\}$ from the current patient S^0 . Then, we can obtain their aligned prostate shapes $\{S_{j \rightarrow 1}^0 | j=1, \dots, t-1\}$ in the planning image (S_1^0) space, the mean prostate shape $\bar{S}^0 = \sum_{j=1}^{t-1} S_{j \rightarrow 1}^0 / (t-1)$, the residual deformation $B_j^0 = S_{j \rightarrow 1}^0 - \bar{S}^0$, and eventually all possible patient-specific prostate deformations for the current patient, i.e., $\{C_j^0 = B_j^0 + S_1^0 | j=1, \dots, t-1\}$. Similarly, the respective non-boundary regional correspondences $\{R_j^0 | j=1, \dots, t-1\}$ can also be obtained with TPS. In this way, we can obtain a set of patient-specific samples, $\{(C_j^0, R_j^0 | j=1, \dots, t-1)\}$, to train a patient-specific correlation model, as done for the training patients in Section 2.2.

Accordingly, our strategy for collecting the statistical correlation and predicting the dense correspondences R_t for the current patient at the t -th time point can be described in Equation (5). We can initially rely more on the population-based correlation model, and then gradually reduce its contribution with the collection of more and more patient-specific information.

$$R_t = (1 - \omega_t) R_t^0 + \omega_t (R_t^0)' \quad (5)$$

$$\omega_t = \begin{cases} 0 & t \leq N_s \\ (t - N_s) / (N_b - N_s) & N_s \leq t \leq N_b \\ 1 & N_b < t \end{cases} \quad (6)$$

Here, R_t^0 denotes the non-boundary regional correspondences predicted by the population-based correlation model as described in Section 2.2, while $(R_t^0)'$ denotes the correspondences predicted by the patient-specific correlation model learned from $t - 1$ treatment images of the current patient. The term $(R_t^0)'$ is not existent for several initial treatment images, simply because the available segmented prostate images for the specific patient are not sufficient to train a statistical correlation model. We can actually begin to train the patient-specific statistical correlation model once N_s time-point images have been obtained. Here, N_s is the minimal number of treatment images for the current patient, and $N_s = 3$ is used in our study. Afterward, we can gradually increase the weight of term $(R_t^0)'$ and simultaneously decrease the weight of term R_t^0 , as more and more new treatment images of the current patient are collected. This can be achieved by defining parameter ω_t according to Equation (6). If we have more than N_b treatment images from the same patient, we can stop using the population-based estimation term R_t^0 , since the patient-specific correlation collected from over N_b treatment images is enough to predict the non-boundary regional correspondence.

Our method for fast correspondence interpolation is summarized as follows:

1. Use the deformable segmentation method to segment prostate from the planning image of a patient under treatment.
2. Linearly align all prostate shape samples of training patients onto the planning image space of the current patient, and then use the aligned samples to learn a population-based correlation model, for capturing the relation between the boundary correspondences and the non-boundary regional correspondences of prostate.
3. For each new treatment image acquired from the current patient, we will first segment the prostate and establish its boundary correspondences with that in the planning image. Then, with the population-based correlation model as well as the established correspondences on the prostate boundary, we can estimate the non-boundary regional correspondences in the prostate of the current patient.
4. With segmentation of more treatment images, we can use them to learn a patient-specific correlation model, to work with the population-based correlation model for correspondence prediction. Once a sufficient number of the treatment images are segmented, the patient-specific correlation model can take over the task for correspondence prediction, without using the population-based correlation model.

3 Experimental Results

The performance of our fast online correspondence interpolation method is tested on serial prostate CT images of 24 patients. Most patients have up to 12 scan images, each with image size of $512 \times 512 \times 61$ and voxel size of $1 \times 1 \times 3\text{mm}^3$. Prostates in all serial images of all patients have been manually segmented by medical expert, and their correspondences have been established with a statistical shape-based method. For comparison, TPS-based correspondence interpolation is used as a baseline method [9, 13]. Both qualitative and quantitative results are reported.

Results on an Individual Patient

Fig. 1 shows the predictive error of prostate deformations in the serial images of a patient by our method, compared to those interpolated by TPS. The top row shows the predictive errors at different treatment times using only the population-based statistical correlation model by setting $\omega_t = 0$ in Equation (5). The bottom row shows the predictive errors using both population-based and patient-specific statistical correlation models. In this figure, the pink contours represent prostate boundaries, while the light-blue outer contour and the white interior contour represent the iso-distance of 15mm from the prostate boundary contour, respectively. According to the color bar in Fig. 1, our fast prediction method can achieve a prediction error of less than 1.0mm.

Fig. 2 shows quantitatively the error distributions for results in Fig. 1. It can be observed that the error distributions in all treatment images are similar to each other when using only the population-based correlation model (red bar). In contrast, the prediction errors are decreased with adding of more and more treatment images of the current patient (blue bar).

Results on All 24 Patients

Table 1 shows the overall predictive errors for all images of all 24 patients by using only the population data, or both population and patient data. The predictive errors on the voxels around 5mm of prostate boundary are calculated, since these voxels locate between prostate and normal tissues where accurate registration is critical for effective treatment, i.e., maximizing the harm to the cancer and minimizing the harm to healthy tissue. It can be observed that the average error is 0.38mm by our method using both population-based and patient-specific statistical correlation, which is much better than 1.02mm obtained by using only the population-based statistical correlation. Also, the maximum error can be reduced significantly by our method.

Table 2 shows the effect on the predictive error with respect to the number of patient's treatment images used for estimating deformation correlation. As we can observe, the predictive error of prostate deformation is reduced with use of more treatment images for learning the patient-specific information.

Speed

The above results demonstrate that our online correspondence interpolation method performs comparable to TPS. For comparing the speed, we load the same prostate boundary landmarks and correspondences into our method and TPS [13] to estimate the dense deformations. As shown in Table 3, when considering larger ROI with the size of $512 \times 512 \times 61$, our method is able to predict the dense deformation field within 24.50 seconds, while TPS needs 6.70 minutes; when considering small ROI with the size of $112 \times 110 \times 93$ exactly around the prostate, it takes 1.85 seconds for our method to estimate the deformation field while TPS needs 25.0 seconds. This result indicates that our method can estimate the dense deformation field in real-time, which has potential to be applied to clinical applications. (OS: 32 bit of Windows 7, CPU: Intel Core 2 Quad Q9400 2.66Hz, Memory: 4GB).

4 Conclusion

We have presented a new fast registration for aligning prostates in the planning image and each treatment image of a patient during radiotherapy, by learning the statistical correlation of the deformations between prostate boundaries and non-boundary regions from both population and patient data. The patient-specific statistical correlation is online-and-incrementally learned from the previous treatment image of the current patient. For the initial treatment images, the population-based statistical correlation plays major function for statistically predicting the dense regional correspondence. As more and more segmented prostate images are obtained from the current patient, the patient-specific statistical correlation starts to take an important role for predicting the dense regional correspondences. Experimental results on real patient data show that our method can produce comparable accuracy as TPS, but it performs much faster than TPS. In the future, we will incorporate our method into the whole pipeline for prostate segmentation and registration, and will further test its overall performance and speed as well.

Acknowledgments

This research was supported by the grant from National Institute of Health (Grant No. 1R01 CA140413). The image data and expert contours used in this study were provided by the Department of Radiation Oncology, UNC-Chapel Hill under support of NIH grants R01 RR018615 and R44/43 CA119571, E.L. Chaney PI. This work was also supported by the grant from National Natural Science Foundation of China (No. 60972102).

References

1. Prostate Cancer Foundation. <http://www.prostatecancerfoundation.org/>.
2. Perez, CA.; Brady, LW.; Halperin, EC.; Schmidt-Ullrich, RK. Principles and Practice of Radiation Oncology. 4th edn.. Lippincott Williams & Wilkins; 2004.
3. Yan D, Lockman D, Brabbins D, Tyburski L, Martinez A. An Off-line Strategy for Constructing a Patient-specific Planning Target Volume in Adaptive Treatment Process for Prostate Cancer. *Int. J. Radiat. Oncol. Biol. Phys.* 2000; 48:289–302. [PubMed: 10925000]
4. Court LE, Tishler RB, Petit J, Cormack R, Chin L. Automatic Online Adaptive Radiation Therapy Techniques for Targets with Significant Shape Change: a Feasibility Study. *Phys. Med. Biol.* 2006; 51:2493–2501. [PubMed: 16675865]
5. Yan D, Jaffray DA, Wong JW. A Model to Accumulate Fractionated Dose in a Deforming Organ. *Int. J. Radiat. Oncol. Biol. Phys.* 1999; 44:665–675. [PubMed: 10348298]
6. Schaly B, Kempe JA, Bauman GS, Battista JJ, Dyk JV. Tracking the Dose Distribution in Radiation Therapy by Accounting for Variable Anatomy. *Phys. Med. Biol.* 2004; 49:791–805. [PubMed: 15070203]
7. Foskey M, Davis B, Goyal L, Chang S, Chaney E, Strehl N, Tomei S, Rosenman J, Joshi S. Large Deformation Three-dimensional Image Registration in Image-Guided Radiation Therapy. *Phys. Med. Biol.* 2005; 50:5869–5892. [PubMed: 16333161]
8. Christensen GE, Rabbitt RD, Miller MI. Deformable Templates Using Large Deformation Kinematics. *IEEE Trans. Image Processing.* 1996; 5:1435–1447.
9. Bookstein FL. Principal Warps: Thin-Plate Splines and the Decomposition of Deformations. *IEEE Trans. Pattern anal. Mach. Intell.* 1989; 11:567–585.
10. Feng Q, Foskey M, Chen W, Shen D. Segmenting CT Prostate Images Using Population and Patient-specific Statistics for Radiotherapy. *Med. Phys.* 2010; 37(8):4121–4132. [PubMed: 20879572]
11. Hotelling H. Relations between Two Sets of Variates. *Biometrika.* 1936; 28:321–377.
12. Liu, T.; Shen, D.; Davatzikos, C. Predictive Modeling of Anatomic Structures Using Canonical Correlation Analysis. *Proceedings of the IEEE International Symposium on Biomedical Imaging; VA, Arlington.* 2004. p. 1279-1282.
13. ITK Insight Toolkit. <http://www.itk.org/>.

Fig. 1.

The distribution of predictive errors at different treatment times by using only the population-based (top row) or both population-based and patient-specific statistical correlation (bottom row). Pink contour represents the shape of prostate boundary, while the light blue and the white contour represents the iso-distance of 15mm from the prostate boundary contour.

Fig. 2.

Overall distributions of predictive errors at 4 different treatment images of a patient, by using only the population-based (red) or both population-based and patient-specific statistical correlation (blue)

Table 1

Comparison of predictive errors on all images of all 24 patients between the method using only population data and the method using both population and patient data

	Mean $\pm$ Std	Minimum	Median	Maximum
Population	1.02 $\pm$ 0.69	0.003	0.88	5.02
Population + Patient-specific	0.38 $\pm$ 0.27	0.001	0.27	3.14

Table 2

The effect on the predictive error with respect to the number of patient's treatment images used for estimation of deformation correlation

Number of patient's treatment images used	Mean $\pm$ Std	Minimum	Median	Maximum
3	0.62 $\pm$ 0.42	0.005	0.53	3.14
4	0.55 $\pm$ 0.37	0.004	0.48	2.37
5	0.45 $\pm$ 0.30	0.002	0.39	1.85
6	0.32 $\pm$ 0.23	0.003	0.27	1.35
7	0.30 $\pm$ 0.24	0.007	0.24	1.72
8	0.27 $\pm$ 0.20	0.007	0.21	1.89
9	0.22 $\pm$ 0.22	0.001	0.17	2.50

Table 3

Comparison the running times for our method and TPS

Prostate data (Number of Landmarks: 816)	TPS	Our method
Large ROI (Size: 512×512×61)	6.70 minutes	24.50 seconds
Small ROI (Size: 112×110×93)	25.00 seconds	1.85 seconds